

**PATENT** 

# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (Case No. 02-434-A)

In the Applic		)	
	Sarah S. Bacus et al.	)	Examiner: Unassigned
Serial No.	10/600,129	)	Crown Art Huit, 1742
Filed:	June 19, 2003	)	Group Art Unit: 1743
	od for Predicting Response to Epidermal th Factor Receptor-Directed Therapy	)	Confirmation No.: 9778
Mail Stop Ar	nendment		
Commission	er for Patents		
P.O. Box 145	50		
Alexandria V	JA 22313-1450		

#### TRANSMITTAL LETTER

In regard to the above identified application,

- 1. We are transmitting herewith the attached:
  - Information Disclosure Statement;
  - Form PTO-1449 including (68 cited references); and
  - Return Postcard
- 2. Applicants believe that no fees are due at this time.
- 3. **GENERAL AUTHORIZATION TO CHARGE OR CREDIT FEES**: Please charge any additional fees or credit overpayment to Deposit Account No. 13-2490. A duplicate copy of this sheet is enclosed.
- 4. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: I hereby certify that I directed that this Transmittal Letter and the correspondence identified above be deposited with the United States Postal Service as "First Class Mail," addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Respectfully submitted,

Date: Aug. 27, 2004

Andrew W. Williams Registration No. 48,644





# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (Case No. 02-434-A)

In the .	Application of:	)
	Sarah S. Bacus et al.	) Examiner: Unassigned
Serial	No. 10/600,129	) ) Group Art Unit: 1743
Filed:	June 19, 2003	)
For:	Method for Predicting Response to Epidermal	) Confirmation No.: 9778
	Growth Factor Receptor-Directed Therapy	)

Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

#### INFORMATION DISCLOSURE STATEMENT

Dear Sir:

Pursuant to the duty of disclosure provided by 37 C.F.R. § 1.56 and §§ 1.97-98, the applicants wish to make all references listed in the PTO-1449 form enclosed herewith of record in the above-identified application. It is requested that each document cited (including any cited in applicant's specification which is not repeated on the attached Form PTO-1449) be given thorough consideration and that it be cited of record in the prosecution history of the present application by initialing on Form PTO-1449. Such initialing is requested even if the Examiner does not consider a cited document to be sufficiently pertinent to use in a rejection, or otherwise does not consider it to be prior art for any reason, or even if the Examiner does not believe that the guidelines for citation have been fully complied with. This is requested so that each document becomes listed on the face of the patent issuing on the present application.

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Portions of the references may be material to the examination of the pending claims, however no such admission is intended. 37 C.F.R. 1.97 (h). The references have not been reviewed in sufficient detail to make any other representation and, in particular, no representation is intended as to the relative importance of any portion of the references. This Statement is not a representation that the cited references have effective dates early enough to be "prior art" within

Respectfully submitted,

McDonnell Boehnen Hulbert & Berghoff LLP

Date: Aug. 27, 2004

the meaning of 35 U.S.C. sections 102 or 103.

3y: \_\_\_\_

Andrew W. Williams

Registration No. 48,644

FORM PTO-1449 (Rex 2422)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.	
3039	INFORMATION DISCLOSURE STATEMENT BY APPLICANT	02-434-A	10/600,129	
AUG 3 0 2004 L	(Use several sheets if necessary)	Applicant:		
A DIALENDON		Sarah S. Bacus et al.		
		Filing Date:	Group:	
		6/19/2003	1743	

# **U.S. PATENT DOCUMENTS**

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
i.	1.	6,235,883	05/22/2001	Jakobovits et al.			

#### **FOREIGN PATENT DOCUMENTS**

	Document Number	Date	Country	Class	Subclass	Trans	slation
						Yes	No

#### OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc).

	2.	Alaoui-Jamali et al., "The role of ErbB-2 tyrosine kinase receptor in cellular intrinsic chemoresistance: mechanisms and implications," Biochem. Cell. Biol., 75:315-325, 1997.
	3.	Albanell et al., "Unraveling Resistance to Trastuzumab (Herceptin): Insulin-Like Growth Factor-I Receptor, a New Suspect," Journal of the National Cancer Institute, Vol 93(24):1830-31, 2001.
	4.	Altiok et al., "Heregulin Induces Phosphorylation of BRCA1 through Phosphatidylinositol 3-Kinase/AKT in Breast Cancer Cells," Journal of Biological Chemistry, 274(5):32274-32278, 1999.
	5.	Arteaga et al., "p <sup>185c-erbB-2</sup> Signaling Enhances Cisplatin-induced Cytotoxicity in Human Breast carcinoma Cells: Association between an Oncogenic Receptor Tyrosine Kinase and Drug-induced DNA Repair," Cancer Research, 54:3758-3765, 1994.
,	6.	Arteaga et al., "The Epidermal Growth Factor Receptor: From Mutant Oncogene in Nonhuman Cancers to Therapeutic Target in Human Neoplasia," J Clinical Oncology, Vol. 1999(18s):32s-40s, 2001.
	7.	Bacus et al., "Neu Differentiation Factor (Heregulin) Induces Expression of Intercellular Adhesion Molecule 1: Implications for Mammary Tumors," Cancer Res. 53:5251-5261, 1993.

EXAMINER	DATE CONSIDERED

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	8.	Bacus et al., "A Ligand for the erbB-2 oncogene Producet (gp30) Induces Differentiation of Human Breast Cancer Cells," Cell Growth & Diff., 3:401-411, 1992.
	9.	Bacus et al., "AKT2 is frequently upregulated in HER-2/neu-positive breast cancers and may contribute to tumor aggressiveness by enhancing cell survival," Oncogene, 21:3532-3540, 2002.
	10.	Bacus et al., "Potential Use of Image Analysis for the Evaluation of Cellular Predicting Factors for Therapeutic Response in Breast Cancers," Analytical and Quantitative Cytology and Histology 19:316-328 (1997).
	11.	Bargmann et al., "Multiple Independent Activations of the neu Oncogene by a Point Mutation Altering the Transmembrane Domain of p185," Cell, Vol. 45:649-657, 1986.
	12.	Baselga et al., "Combined anti-EGF receptor and anti-HER2 receptor therapy in breast cancer: a promising strategy ready for clinical testing," Annuals of Oncology 13:8-9, 2002.
	13.	Baselga et al., "Receptor Blockade with Monoclonal Antibodies as Anti-Cancer Therapy," Pharmacol Ther 64:127-154, 1994.
	14.	Basso et al, "Ansamycin antibiotics inhibit Akt activation and cyclin D expression in breast cancer cells that overexpress HER2," Oncogene, 21:1159-1166, 2002.
ý	15.	Bruns et al., "Blockade of the Epidermal Growth Factor Receptor Signaling by a Novel Tyrosine Kinase Inhibitor Leads to Apoptosis of Endothelial Cells and Therapy of Human Pancreatic Carcinoma," Cancer Research, 60:2926-2935, (2000).
•	16.	Carpenter et al., "Epidermal Growth Factor," An. Review Biochem., 48:193-216, 1979.
	17.	Carraway et al., "The erbB3 Gene Product Is a Receptor for Heregulin," Journal Biological Chemistry, 269(19):14303-14306, 1994.
	18.	Carter et al, "Humanization of an anti-p185 <sup>HER2</sup> antibody for human cancer therapy," Proc. Natl Acad Sci USA 89:4285-4289, 1992.
	19.	Christensen et al, "High Levels of HER-2 Expression Alter the Ability of Epidermal Growth Factor Receptor (EGFR) Family Tyrosine Kinase Inhibitors to Inhibit EGFR Phosphorylation <i>in Vivo</i> ," Clinical Cancer Research, Vol. 7:4230-4238, 2001.
·	20.	Cobleigh et al., "Multinational Study of the Efficacy and Safety of Humanized Anti-HER2 Monoclonal Antibody in Women Who Have HER2-Overexpressing Metastatic Breast Cancer That Has Progressed After Chemotherapy for Metastatic Disease," Journal of Clinical Oncology 17(9):2639-2648 (1999).
	21.	Coussens et al., "Tyrosine Kinase Receptor with Extensive Homology to EGF Receptor Shares Chromosomal Location with neu Oncogene," Science, 230(4730):1130-1139, 1985.
	22.	Demitri et al.; "Efficacy and Safety of IMATINIB Mesylate in Advanced Gastrointestinal Stromal Tumors," New England Journal of Medicine 347(7):472-480 (2002).
	23.	Druker et al., "Efficacy and Safety of Specific Inhibitor of the BCR-ABL Tyrosine Kinase in Chronic Myeloid Leukemia," New England Journal of Medicine 344(14):1031-1037 (2001).
	24.	Erlichman et al., "the HER Tyrosine Kinase Inhibitor CI1033 Enhances Cytotoxicity of 7-Ethyl-10-hydroxycamptothecin and Topotecan by Inhibiting Breast Cancer Resistance Protein-mediated Drug Efflux," Cancer Research 61:739-748, 2001.
	25.	Fujimoto-Ouchi et al, "Antitumor activity of combinations of anti-HER-2 antibody trastuzumab and oral fluoropyrimidines capecitabine/5'-dFUrd in human breast cancer models," Cancer Chemother Pharmacol, 49:211-216, 2002.

EXAMINER	DATE CONSIDERED

	26.	Fujimura et al., "Selective Inhibition of the Epidermal Growth Factor Receptor by ZD1839 Decreases the Growth and Invasion of Ovarian Clear Cell Adenocarcinoma Cells," Clinical Cancer Research, Vol. 8:2448-2454, 2002.
	27.	Fukazawa et al., "Tyrosine Phosphorylation of Cbl upon Epidermal Growth Factor (EGF) Stimulation and Its Association with EGF Receptor and Downstream Signaling Proteins," Journal of Biological Chemistry 271(24):14554-14559 (1996).
	28.	Hackel et al., "Epidermal growth factor receptors: critical mediators of multiple receptor pathways," Curr. Opin. Cell Biol. 11:184-189 (1999).
	29.	Hancock et al., "A Monoclonal Antibody against the c-erbB-2 Protein Enhances the Cytotoxicity of cis- Diamminedichloroplatinum against Human Breast and Ovarian Tumor Cell Lines," Cancer Research, 51:4575-4580, 1991.
- J1877 - Living	30.	Herbst et al., "Selective Oral Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor ZD1839 Is Generally Well-Tolerated and Has Activity in Non-Small-Cell Lung Cancer and Other Solid Tumors: Results of a Phase I Trial," Journal of Clincal Oncology, Vol. 20(18):3815-3825, 2002.
	31.	Hidalgo et al, "Phase I and Pharmacologic Study of OSI-774, an epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor, in Patients With Advanced Solid Malignancies," Journal of Clinical Oncology, Vol 19(13):3267-3279, 2001.
1	32.	Holmes et al, "Identification of Heregulin, a Specific Activator of p185 <sup>erbB2</sup> ," Science, 256(5060):1205-1210, 1992.
•	33.	Huang et al., "Modulation of Radiation Response after Epidermal Growth Factor Receptor Blockade in Squamous Cell Carcinomas: Inhibition of Damage Repair, Cell Cycle Kinetics, and Tumor Angiogenesis," Clinical Cancer Res., Vol. 7:2166-2174, 2000.
	34.	Hudziak et al., "p185 <sup>HER2</sup> Monoclonal Antibody Has Antiproliferative Effects In Vitro and Sensitizes human Breast Tumor Cells to Tumor Necrosis Factor," Mol. Cell. Biol., 9:1165-1172, 1989).
•	35.	Klapper et al., "Tumor-inhibitory Antibodies to HER-2/ErbB-2 May Act by Recruiting c-Cbl and Enhancing Ubiquitination of HER-2," Cancer Research, 60:3384-3388, 2000.
	36.	Klapper et al., "A subclass of tumor-inhibitory monoclonal antibodies to ErbB-2/HER2 blocks crosstalk with growth factor receptors," Oncogene 14:2099-2109, 1997.
	37.	Kraus et al., "Isolation and characterization of <i>ERBB3</i> , a third member of the <i>ERBB</i> / epidermal growth factor receptor family: Evidence for overexpression in a subset of human mammary tumors," Proc. Natl. Acad. Sci. USA, 86:9193-9197, 1989.
	38.	Lange et al., "Convergence of Progesterone and Epidermal Growth Factor Signaling in Breast Cancer," Journal of Biological Chemistry 273(47):31308-31316 (1998).
	39.	Liu et al., "Heregulin Regulation of Akt/Protein Kinase B in Breast Cancer Cells," Biochemical and Biophysical Research Communications, 261:897-903, 1999.
	40.	Mendelsohn & Baselga, "The EGF receptor family as targets for cancer therapy," Oncogene 19:6550-6565 (2000).
	41.	Mendelsohn, "The epidermal growth factor receptor as a target for therapy with antireceptor monoclonal antibodies," Seminars in Cancer Biology, Vol. 1:339-344, 1990.
	42.	Moasser et al, "The Tyrosine Kinase Inhibitor ZA1839 ("Iressa") Inhibits HER2-driven Signaling and Suppresses the Growth of HER2-overexpressing Tumor Cells," Cancer Research, 61:7184-7188, 2001.
-	43.	Munster et al., "Degradation of HER2 by Ansamycins Induces Growth Arrest and Apoptosis in Cells with HER2 Overexpression via a HER3, Phosphatidylinositol 3'-Kinase-AKT-dependent Pathway," Cancer Research 62:3132-3137, 2002.

EXAMINER	DATE CONSIDERED

	44.	Normanno et al, "Cooperative inhibitory effect of ZA1839 (Iressa) in combination with trastuzumab (Herceptin) on human breast cancer cell growth," Annals of Oncology, 13:65-72, 2002.
	45.	Olayioye et al., "ErbB-1 and ErbB-2 Acquire Distinct Signaling Properties Dependent upon Their Dimerization partner," Molecular and Cellular Biology 18(9):5042-5051 (1998).
	46.	Peles et al., "Isolation of the Neu/HER-2 Stimulatory Ligand: A 44 kd Glycoprotein That Induces Differentiation of Mammary Tumor Cells," Cell, 69:205-216, 1992.
	47.	Peles et al., "Cell-type specific Interaction of Neu differentiation factor (NDF/heregulin) with Neu/HER-2 suggests complex ligand – receptor relationships," EMBO Journal; 12(3):961-71, 1993.
	48.	Pietras et al., "Antibody to HER-2/neu receptor blocks DNA repair after cisplatin in human breast and ovarian cancer cells," Oncogene, 9:1829-1838, 1994.
	49.	Pinkas-Kramarski et al., "The oncogenic ErbB-2/ErbB-3 heterodimer is a surrogate receptor of the epidermal growth factor and betacellulin," Oncogene, 16:1249-1258, 1998.
	50.	Pinkas-Kramarski et al., "Brain neurons and glial cells express Neu differentiation factor / heregulin: A survival factor for astrocytes," Proc. Natl. Acad. Sci. USA, 91:9387-9391, 1994.
•	51.	Pinkas-Kramarski et al., "Neu Differentiation Factor/Neuregulin Isoforms Activate Distinct Receptor Combinations," The Journal of Biological Chemistry, Vol. 271(32):19029-19032, 1996.
•	52.	Plowman et al., "Heregulin Induces tyrosline phosphorylation of HER4/p180 <sup>erbB4</sup> ," Nature, 366:473-475, 1993.
	53.	Sachs et al., "Cell Differentiation and Bypassing of Genetic Defects in the Suppression of Malignancy," Cancer Res., 47:1981-1986, 1987.
	54.	Semba et al., "A v-erbB-related protooncogene, c-erbB-2, is distinct from the c-erbB-1/epidermal growth factor-receptor gene and is amplified in a human salivary gland adenocarcinoma," Proc. Natl. Acad. Sci., 82:6497-6501, 1985.
	55.	Shak, "Overview of the Trastuzumab (Herceptin) Anti-HER2 Monoclonal Antibody Clinical Program in HER2-Overexpressing Metastatic Breast Cancer," Seminars in Oncology, Vol. 26(4, Suppl 12):71-77, 1999.
	56.	Slamon et al., "Human Breast Cancer: Correlation of Relapse and Survival with Amplification of the HER-2/neu Oncogene," Science, 235(4785):177-182, 1987.
	57.	Sliwkowski et al, "Nonclinical Studies Addressing the Mechanism of Action of Trastuzumab (Herceptin)," Seminars in Oncology, 26(4, Suppl 12):60-70, 1999.
	58.	Stancovski et al., "Mechanistic aspects of the opposing effects of monoclonal antibodies to the ERBB2 receptor on tumor growth," Proc Natl Acad Sci USA 88:8691-8695, 1991.
	59.	Tagliabue et al., "Selection of monoclonal antibodies which induce internalization and phosphorylation of p185 <sup>HER2</sup> and growth inhibition of cells with HER2 <i>INEU</i> gene amplification," Int. J. Cancer, 47:933-937, 1991.
	60.	Tzahar et al., "ErbB-3 and ErbB-4 Function as the Respective Low and High Affinity Receptors of All Neu Differentiation Factor/Heregulin Isoforms," Journal of Biological Chemistry, 269(40):25226-25233, 1994.
	61.	Tzahar et al., "A Hierarchical Network of Interreceptor Interactions Determines Signal Transduction by Neu Differentiation Factor/Neuregulin and Epidermal Growth Factor," Molecular and Cellular Biology 16(10):5276-5287 (1996).
	62.	Vogel et al., "Efficacy and Safety of Trastuzumab as a Single Agent in First-Line Treatment of <i>HER2</i> -Overexpressing Metastatic Breast Cancer," Journal of Clinical Oncology, Vol 20(3):719-726, 2002.

EXAMINER	DATE CONSIDERED

63.	63. Vogel et al., "First-Line Herceptin <sup>®</sup> Monotherapy in Metastatic Breast Cancer," Oncology, 61(suppl 2):37-42, 2001.	
 64.	Xia et al. "Anti-tumor activity of GW572016: a dual tyrosine kinase inhibitor blocks EGF activation of EGFR/erbB2 and downstream Erk1/2 and AKT pathways," Oncogene 21:6255-6263 (2002).	
65.	Xing et al., "The Ets protein PEA3 suppresses <i>HER-2/neu</i> overexpression and inhibits tumorigenesis," Nature Med., 6:189-195, 2000.	
66.	Yang X et al., "Development of ABX-EGF, a fully human anti-EGF receptor monoclonal antibody, for cancer therapy," Crit Rev Oncol Hemato 38(1):17-23 (2001).	
 67.	Yang et al., "Eradication of Established Tumors by a Fully Human Monoclonal Antibody to the Epidermal Growth Factor Receptor without Concomitant Chemotherapy," Cancer Research 59(6):1236-1243 (1999).	
68.	Ye et al., "Augmentation of a humanized Anti-HER2 mAb 4D5 induced growth inhibition by a human-mouse chimeric anti-EGF receptor mAb C225," Oncogene, 18:731-738, 1999.	

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